

Amendments to the Specification:

Please amend the paragraph beginning at page 35, line 32 as follows:

The inventor found that wild-type Fn3 is more stable at acidic pH than at neutral pH (Koide *et al.*, 1998). The pH dependence of Fn3 stability is characterized in FIG. 18. The pH dependence curve has an apparent transition midpoint near pH 4 (FIG. 18). These results suggest that by identifying and removing ~~destabilizing~~ destabilizing interactions in Fn3 one is able to improve the stability of Fn3 at neutral pH. It should be noted that most applications of engineered Fn3, such as diagnostics, therapeutics and catalysts, are expected to be used near neutral pH, and thus it is important to improve the stability at neutral pH. Studies by other investigators have demonstrated that the optimization of surface electrostatic properties can lead to a substantial increase in protein stability (Perl *et al.* 2000, Spector *et al.* 1999, Loladze *et al.* 1999, Grimsley *et al.* 1999).

Please amend the paragraph beginning at page 76, line 6 as follows:

The carboxyl triad (Asp 7 and 23, and Glu 9) is highly conserved in FNfn10 from nine different organisms that were available in the protein sequence databank at National Center for Biotechnology Information (~~www.ncbi.nlm.nih.gov~~). In these FNfn10 sequences, Asp 9 is conserved except one case where it is replaced with Asn, and Glu 9 is completely conserved. The position 23 is either Asp or Glu, preserving the negative charge. As was discovered in this study, the interactions among these residues are destabilizing. Thus, their high conservation, despite their negative effects on stability, suggests that these residues have functional importance in the biology of fibronectin. In the structure of a four-FN3 segment of human fibronectin (Leahy, D. J., Aukhil, I. & Erickson, H. P. (1996) *Cell* 84, 155-164), these residues are not directly involved in interactions with adjacent domains. Also these residues are located on the opposite face of FNfn10 from the integrin-binding RGD sequence in the FG loop (FIG. 21). Therefore, it is not clear why these destabilizing residues are almost completely conserved in FNfn10. In contrast, no other FN3 domains in human fibronectin contain this carboxyl triad (for a sequence alignment, see ref Main, A. L., Harvey, T. S., Baron, M., Boyd, J. & Campbell, I. D. (1992) *Cell*

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71, 671-678). The carboxyl triad of FNfn10 may be involved in important interactions that have not been identified to date.